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Commentary

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Beneficial and Therapeutic Potential of Ketone Bodies (KB) in Clinical Practice

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Abstract

Various discussion exists concerning ketone bodies (KB) for beneficial effects. In 2021, the American College of Cardiology (ACC) has presented the therapeutic potential of KB for cardiovascular (CV) disease. KB cover 10-15% of cardiac production of ATP, elevation of cardiac energetics, and reduction of cardiac remodeling, inflammation, and oxidative stress.

Keywords

Ketone Bodies, American College of Cardiology, Low Carbohydrate Diet, Cardiovascular, B-Hydroxybutyrate

Abbreviations

KB: Ketone Bodies; ACC: American College of Cardiology; LCD: Low Carbohydrate Diet; CV: Cardiovascular; β HB: β -hydroxybutyrate

From human medical point of view, nutritional changes may influence to several aspects. They include macroscopic dietary interventions such as Low Carbohydrate Diet (LCD), Ketogenic Diet (KD), Calorie Restriction (CR), a high-fat meal [1]. LCD and KD bring elevated ketone bodies (KB) in the blood, hyperketonemia [2]. Various discussion exists concerning whether KB would cause risky or beneficial situation. In 2021, the American College of Cardiology (ACC) has presented the therapeutic potential of KB for cardiovascular (CV) disease [3].

KB has been evaluated to be the main mediators of metabolic health. Multiple beneficial efficacies of KD,

neuronal pathology, impacting metabolism, and tumorigenesis have been investigated in both animal and human clinical research [4]. KB are produced endogenously in the liver, and are acting pleiotropically as signaling molecules and metabolic intermediates.

Generally, KB seem to show beneficial effects for broad system of human body. KB may give supplemental fuel to the energy-lacked heart, and this efficacy to CV axis seems to develop far beyond the expected cardiac energy level [3]. From a variety of research, KB have several evidences to influence various cellular processes. They include CV risk

factors, cardiac remodeling, endothelial function, oxidative and inflammation stresses, and gene transcription. Recent reviews have revealed the pleiotropic and bioenergetic efficacy of KB, which can probably attribute for its CV beneficial mechanism with several human and animal evidences.

Regarding cardiac function, hyperketonemia can especially cause several beneficial mechanisms [3]. Related factors may include i) elevation of cardiac energetics, endothelial function mitochondrial function, ii) reduction of cardiac remodeling, inflammation, oxidative stress, Histone deacetylase (HDAC), iii) related mechanism of blood pressure, body weight, blood glucose and lipid profile.

KB become major source for production of ATP during stress situation, so as to hold bioenergetic homeostasis in the heart, brain and muscles. In our heart, KB cover 10-15% of cardiac production of ATP, where the detail contribution is not clarified yet [5]. According to several studies, the failing heart with heart failure has been reported to rely more on KB as effective energy source than previously suggested. Moreover, it is suggested that KB play a role of signaling molecules which can reduce cardiac and systemic inflammatory situation [6]. Consequently, intentionally increasing circulating KB can possibly cause beneficial efficacy for adjunct therapy for heart failure.

Furthermore, plasma β -hydroxybutyrate (β HB, 3-Hydroxybutyric Acid, 3-OHBA) and its utilization in the heart have been increased for patients with diabetes and arrhythmogenic cardiomyopathy. This fact suggests that the shift to KB would be standard heart response to various stress [7]. In the experiment of murine model of HRrEF, the oxidation of KB is found about 20% of energy production in the heart [8].

Recently, sodium-glucose cotransporter-2 inhibitors (SGLT2i) has been widely used for stimulating glucose excretion and been recognized for its CV benefits in heart failure patients with/without diabetes [9]. CV beneficial mechanism for SGLT2i may be mediated by the elevated circulating KB [10]. In summary, KB exert protective efficacy for CVD, and exogenous ketones

administration to human may be an alternative way to KD for beneficial KB in the future.

Conflict of Interest

The author has read and approved the final version of the manuscript. The author has no conflicts of interest to declare.

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